DETAILED ACTION

Claims *1*-38*, 40-53, 55-57,64-66 and 69-89* are pending.

Claims 1-3, 5-20, 27-37, 49-53, 55-57, 64-66, 69-75 are withdrawn.

Claims 4, 21-26, 38, 40-48, 76-89 are examined.

Any rejection of record in the previous action not addressed in this office action is withdrawn..

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 21- 26, 38, 41- 43, 45-48, 76- 79, 81, 82, 88, 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Tuite et al (WO 93/25676) (newly cited by applicants).

Tuite et al. discloses a 2 micron plasmid comprising the PDI gene, and a gene encoding a non 2-micron gene (see page 68-72). The reference discloses a host cell, which is S. cerevisiae, comprising the plasmid (page 72, 68-69). The reference also discloses host cells comprising a PDI gene, integrated into the genome, and a gene encoding "trasnferrin based protein", on a plasmid, or integrated, at any location, since

any protein meets the limitation of a variant of transferrin (page 64-67, for example). It is noted that the recitation in claim 80 of "a sequence of transferrin" encompasses embodiments having only 2 amino acids (a sequence) in common with transferrin, and therefore encompasses most any protein. The reference discloses that mammalian protein disulfide isomerase may be the PDI, which is not produced in yeast unless the mammalian PDI gene is present.

Claims 4, 21, 22, 24-26, 38, 41-48, 76-79, 81, 88, 89, are rejected under 35 U.S.C. 102(b) as being anticipated by Shusta et al. (Nature Biotechnol. 16, 773-777 (1998) (cited by applicants).

This rejection is maintained in part and is a new rejection in part, due to new reasoning and new rejection of claims.

It is noted preliminarily that the term "transferrin-based protein" or "a variant or fragment thereof or a fusion protein comprising transferrin, a variant or fragment thereof" encompasses virtually any protein. Shusta et al. disclose a 2 micron family plasmid, which is 2micron plasmid, comprising a gene encoding peptide disulphide isomerase and a gene encoding a non-2 micron family plasmid protein, and yeast S. cerevisiae cells transformed with said plasmid (see page 776, second column, lines 20-36; see page 775, second column, first paragraph)(claims 4, 21,22, 24-26, 38, 41-48, 76-79, 81, 82, 88, 89). Shusta et al. disclose a host cell comprising a recombinant gene encoding PDI which is chromosomally integrated in tandem with the endogenous copy, such that the level of PDI production is increased, (page 776, second col. line 33-36) and a copy of a gene encoding a transferrin-based protein or variant of transferrin,

which is disclosed to be either chromosomally integrated or on a plasmid (see page 773, second col. second paragraph). It is noted that the term "recombinant" does not distinguish over a naturally occurring product, such as a gene or protein which is present in a native or non-recombinant cell. It is noted that since transferrin-based protein encompasses virtually any protein (since it is defined as any variant or fragment of a transferrin protein), and since a gene encoding a "transferrin-binding protein" is present in the chromosome of S. cerevisiae adjacent to the PDI gene, the native S. cerevisiae cell would meet the limitation of a host cell comprising a gene "chromosomally integrated at the locus of an endogenously encoded PDI gene without disrupting the expression of the endogenous PDI gene", as recited in claims 44, 48, 79, 82. Regarding claim 80, it is noted that the recitation in claim 80 of "a sequence of transferrin" encompasses embodiments having only 2 amino acids (a sequence) in common with transferrin, and therefore encompasses most any protein.

This rejection is maintained in part for the reasons set forth in the previous Office action, mailed 12/14/10. Applicant's arguments filed 6/14/ 11 have been considered but have not been found convincing. Applicants have argued that claim 38 is not anticipated because "the term "transferrin-based protein" is expressly defined in the specification and is clear as noted above", and that "scFv of Shusta does not fall within this express definition". However, the definition in the specification noted by applicants at page 16-17 of arguments, includes "variant or fragment thereof or a fusion protein

comprising transferrin, a variant or fragment thereof". This encompasses virtually any protein, including any protein disclosed by Shusta et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 40, 80, are rejected under 35 U.S.C. 103(a) as being unpatentable over Shusta et al. . (Nature Biotechnol. 16, 773-777 (1998) (cited by applicants), or Tuite et al (WO 93/25676) in view of Funk et al. (WO 92/13550).

Shusta et al. or Tuite et al. are cited essentially for the reasons set forth above. The difference between the references and the instant claims is that human transferrin is the second transferrin based protein. However, Funk et al. disclose the human transferrin encoding gene, and disclose the expression of said gene in eukaryotic cells (see abstract, see page 2-3; see claims). It would have been obvious to one of ordinary skill in the art to have used the plasmids and host cells comprising PDI gene, disclosed by Shusta et al., and Tuite et al., for the expression of the human transferrin gene, disclosed by Funk, since yeast cells are well known to be useful for expression of heterologous genes, and since Funk et all. Disclose that the trasnferrin protein contain a large number of disulfide bridges. One would be motivated by the desire to produce function transferrin protein having disulfide bridges efficiently formed by PDI.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 87, 84-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 87 is vague and indefinite in the recitation of "the recombinant gene encoding PDI is on a plasmid and the recombinant gene encoding PDI is chromosomally integrated". It is not clear how a single gene is both on a plasmid, and is chromosomally integrated. Therefore the claim is indefinite.

Claims 84-86 are vague and indefinite in the dependence on claim 92. There is no claim 92 in the claims, and therefore it cannot be determined what is intended by the claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 4:30, Monday - Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

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